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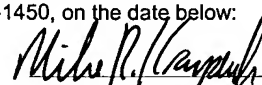
May 18, 2004

**CERTIFICATE OF MAILING**  
37 C.F.R. 1.8

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May 18, 2004

Date

  
Michael R. Krawzsenek

**MS AMENDMENT**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, Virginia 22313-1450

RE: *U.S. Patent Application No. 10/671,340 entitled "MODIFIED GPL-1 PEPTIDES WITH INCREASED BIOLOGICAL POTENCY" – Denis Gravel et al.*  
*Our reference: GOUD:038US*  
*Client reference: ES/11718.104*

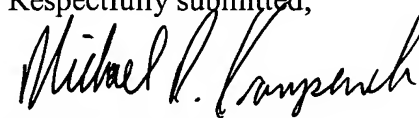
Sir:

Enclosed for filing in the above-referenced patent application is an Information Disclosure Statement, Form PTO-1449, and references A1-A2, B1-B3 and C1-C32.

No fees are believed to be due in connection with the filing of this Information Disclosure Statement, however, should any fees under 37 C.F.R. §§ 1.16 to 1.21 be deemed necessary for any reason relating to the enclosed materials, the Commissioner is authorized to deduct the appropriate fees from Fulbright & Jaworski Deposit Account No.: 50-1212/GOUD:038US.

Please date stamp and return the enclosed postcard evidencing receipt of these materials.

Respectfully submitted,



Michael R. Krawzsenek  
Reg. No. 51,898

MRK/kmv  
Encl.: as noted



PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Re Application of:  
Denis Gravel *et al.*

Serial No.: 10/671,340

Filed: September 25, 2003

For: MODIFIED GPL-1 PEPTIDES WITH  
INCREASED BIOLOGICAL POTENCY

Group Art Unit: 1614

Examiner: Unknown

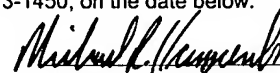
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May 18, 2004

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Michael R. Krawzsenek

INFORMATION DISCLOSURE STATEMENT

**MS AMENDMENT**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, Virginia 22313-1450

Sir:

In compliance with the duty of disclosure under 37 C.F.R. § 1.56, it is respectfully requested that this Information Disclosure Statement be entered and the documents listed on attached Form PTO-1449 be considered by the Examiner and made of record. Copies of the listed documents required by 37 C.F.R. § 1.98(a)(2) are enclosed for the convenience of the Examiner.

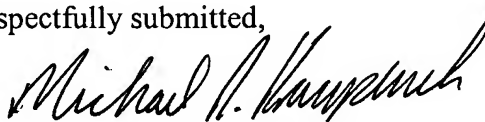
In accordance with 37 C.F.R. §§ 1.97(g), (h), this Information Disclosure Statement is not to be construed as a representation that a search has been made, and is not to be construed to be

an admission that the information cited is, or is considered to be, material to patentability as defined in 37 C.F.R. § 1.56(b).

The present Information Disclosure Statement is being filed prior to the receipt of a first Official Action reflecting an examination on the merits, and hence is believed to be timely filed in accordance with 37 C.F.R. § 1.97(b). No fees are believed to be due in connection with the filing of this Information Disclosure Statement, however, should any fees under 37 C.F.R. §§ 1.16 to 1.21 be deemed necessary for any reason relating to these materials, the Commissioner is authorized to deduct the appropriate fees from Fulbright & Jaworski Deposit Account No.: 50-1212/GOUD:038US.

Applicants respectfully request that the listed documents be made of record in the present case.

Respectfully submitted,



Michael R. Krawzsenek  
Reg. No. 51,898  
Attorney for Applicants

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Date: May 18, 2004

Form PTO-1449 (modified)

Atty. Docket No.

GOUD:038US

Serial No.

10/671,340

List of Patents and Publications for Applicant's

Applicant

Denis Gravel *et al.*

INFORMATION DISCLOSURE STATEMENT

Filing Date:

September 25, 2003

Group:

1614

(Use several sheets if necessary)

U.S. Patent Documents

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Foreign Patent Documents

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Other Art

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## U.S. Patent Documents

Exam. Init.	Ref. Des.	Document Number	Date	Name	Class	Sub Class	Filing Date of App.
	A1	5,512,549	4/30/96	Chen <i>et al.</i>	514	12	10/18/94
	A2	5,545,618	8/13/96	Buckley <i>et al.</i>	514	12	12/10/93

## Foreign Patent Documents

Exam. Init.	Ref. Des.	Document Number	Date	Country	Class	Sub Class	Translation Yes/No
	B1	EP 0 733 644	9/25/96	Europe			English
	B2	WO 91/11457	8/08/91	PCT			English
	B3	WO 99/43707	9/02/99	PCT			English

## Other Art (Including Author, Title, Date Pertinent Pages, Etc.)

Exam. Init.	Ref. Des.	Citation
	C1	Adelhorst <i>et al.</i> , "Structure-activity studies of glucagon-like peptide-1," <i>J. Biol. Chem.</i> , 269(9):6275-6278, 1994.
	C2	Burcelin <i>et al.</i> , "Long-lasting antidiabetic effect of a dipeptidyl peptidase IV-resistant analog of glucagon-like peptide-1," <i>Metabolism</i> , 48(2):252-258, 1999.
	C3	D'alessio <i>et al.</i> , "Glucagon-like peptide 1 decreases hepatic glucose production independent of insulin and glucagon," <i>Diabetes</i> , 46(suppl 1):29A, 1997.
	C4	Deacon <i>et al.</i> , "Dipeptidyl peptidase IV resistant analogues of glucagon-like peptide-1 which have extended metabolic stability and improved biological activity," <i>Diabetologia</i> , 41:271-278, 1998.
	C5	Doyle and Egan, "Glucagon-like peptide-1," <i>Recent Prog. Horm. Res.</i> , 56:377-399, 2001.
	C6	Doyle <i>et al.</i> , "Insertion of an N-Terminal 6-aminohexanoic acid after the 7 amino acid position of glucagon-like peptide-1 produces a long-acting hypoglycemic agent," <i>Endocrinology</i> , 142(10):4462-4468, 2001.
	C7	Drucker, "Minireview: the glucagon-like peptides," <i>Endocrinology</i> , 142(2):521-527, 2001.

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Form PTO-1449 (modified)

Atty. Docket No.

GOUD:038US

Serial No.

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Applicant

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U.S. Patent Documents

See Page 1

Foreign Patent Documents

See Page 1

Other Art

See Page 1

## Other Art (Including Author, Title, Date Pertinent Pages, Etc.)

Exam. Init.	Ref. Des.	Citation
	C8	Dugas and Penney, In: <i>Bioorganic Chemistry</i> , Springer-Verlag, NY, 54-92, 1981.
	C9	Gorrell <i>et al.</i> , "CD26: a multifunctional integral membrane and secreted protein of activated lymphocytes," <i>Scand. J. Immunol.</i> , 54:249-264, 2001.
	C10	Gutniak <i>et al.</i> , "Antidiabetogenic effect of glucagon-like peptide-1 (7-36)amide in normal subjects and pateints with diabetes mellitus," <i>The New England Journal of Medicine</i> , 326:1316-1322, 1992.
	C11	Gutniak, "Treatment of diabetes GLP-1: a new kid in town," <i>International Diabetes Monitor</i> , 9(2):1-12, 1997.
	C12	Holst, "Glucagonlike peptide 1: a newly discovered gastrointestinal hormone," <i>Gastroenterology</i> , 107:1848-1855, 1994.
	C13	Holst, "Glucagon-like peptide 1 (GLP-1): an intestinal hormone, signaling nutritional abundance, with an unusual therapeutic potential," <i>Trends Endocrinol. Metab.</i> , 10(6):229-235, 1999.
	C14	Holz <i>et al.</i> , "Activation of a cAMP-regulated Ca <sup>2+</sup> signaling pathway in pancreatic $\beta$ -cells by the insulinotropic hormone glucagon-like peptide-1," <i>J. Biol. Chem.</i> , 270(30):17749-17757, 1995.
	C15	Kieffer and Habener, "The glucagon-like peptides," <i>Endocrine Reviews</i> , 20(6):876-913, 1999.
	C16	Kreymann <i>et al.</i> , "Glucagon-like peptide-1 7-36: a physiological incretin in man," <i>Lancet</i> , 2(8571):1300-1304, 1987.
	C17	Merrifield, "Solid phase peptide synthesis. I. The synthesis of a tetrapeptide," <i>Chem. Soc.</i> , 85:2149-2154, 1962.
	C18	Nauck <i>et al.</i> , "Reduced incretin effect in Type 2 (non-insulin-dependent) diabetes," <i>Diabetologia</i> , 29:46-52, 1986.
	C19	Nauck <i>et al.</i> , "Normalization of fasting hyperglycaemia by exogenous glucagon-like peptide 1(7-36 amide) in type 2 (non-insulin-dependent) diabetic patients," <i>Diabetologia</i> , 36:741-744, 1993.
	C20	Nauck, "Glucagonlike peptide 1," <i>Curr. Opin. Endocrinol. Diabet.</i> , 4:291-299, 1997.
	C21	Peptide synthesis protocols, <i>Methods in molecular biology</i> , Vol. 35, Pennington and Dunn (eds.), Humana Press, 1994.

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Form PTO-1449 (modified)		Atty. Docket No. GOUD:038US	Serial No. 10/671,340
List of Patents and Publications for Applicant's  INFORMATION DISCLOSURE STATEMENT  (Use several sheets if necessary)		Applicant Denis Gravel <i>et al.</i>	
		Filing Date: September 25, 2003	Group: 1614
U.S. Patent Documents <i>See Page 1</i>	Foreign Patent Documents <i>See Page 1</i>	Other Art <i>See Page 1</i>	

### Other Art (Including Author, Title, Date Pertinent Pages, Etc.)

Exam. Init.	Ref. Des.	Citation
	C22	Perfetti and Merkel, "Glucagon-like peptide-1: a major regulator of pancreatic $\beta$ -cell function," <i>European Journal of Endocrinology</i> , 143:717-725, 2000.
	C23	<i>Remington's Pharmaceutical Sciences</i> , 15 <sup>th</sup> ed., 33:624-652, Mack Publishing Company, Easton, PA, 1980.
	C24	Scrocchi <i>et al.</i> , "Glucose intolerance but normal satiety in mice with a null mutation in the glucagon-like peptide 1 receptor gene," <i>Nature Medicine</i> , 2(11):1254-1258, 1996.
	C25	Siegel <i>et al.</i> , "Biological activity of GLP-1-analogues with N-terminal modifications," <i>Regulatory Peptides</i> , 79:93-102, 1999.
	C26	Stewart and Young, In: <i>Solid Phase Peptide Synthesis</i> , 24-66, Freeman, San Francisco, 1969.
	C27	Suzuki <i>et al.</i> , "Effects of GLP-1 and its fragment peptides on pancreatic hormone release," <i>Diabetes Res.</i> , 5(Suppl 1):S30, 1988.
	C28	Toft-Nielsen <i>et al.</i> , "Continuous subcutaneous infusion of glucagon-like peptide 1 lowers plasma glucose and reduces appetite in type 2 diabetic patients," <i>Diabetes Care</i> , 22:1137-1143, 1999.
	C29	Tolessa <i>et al.</i> , "Inhibitory effect of glucagon-like peptide-1 on small bowel motility," <i>J. Clin. Invest.</i> , 102(4):764-774, 1998.
	C30	Wang <i>et al.</i> , "Glucagon-like peptide-1 can reverse the age-related decline in glucose tolerance in rats," <i>J. Clin. Invest.</i> , 99(12):2883-2889, 1997.
	C31	Xiao <i>et al.</i> , "Biological activities of glucagon-like peptide-1 analogues in vitro and in vivo," <i>Biochemistry</i> , 40:2860-2869, 2001.
	C32	Xu <i>et al.</i> , "Exendin-4 stimulates both $\beta$ -cell replication and neogenesis, resulting in increased $\beta$ -cell mass and improved glucose tolerance in diabetic rats," <i>Diabetes</i> , 48:2270-2276, 1999.

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